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Letter to the editor

On modeling the causes of presbyopia

Weale (2000) presents a theoretical analysis to support his contention for a multifactorial explanation for presbyopia. He suggests that the model supports the notion that the accelerated loss of accommodation relative to other physiological indicators of age is due to the combined effect of normal age related changes in the component elements of the accommodative apparatus.

Weale's model considers age changes in the ratio of Young's modulus of elasticity of the lens and capsule, capsular thickness, the ratio of the lens major and minor axes and the anterior lens radius of curvature. These parameters are used to compute lens/capsular stress and thereby changes in lens anterior surface curvature and accommodation. Weale (2000) suggests his model predicts the progression of presbyopia shown by Brückner, Batschelet, and Hugenschmidt (1987) and argues that it demonstrates that lens hardening (or any other single factor) cannot be considered as a predominant cause of presbyopia.

Glasser and Campbell (1998) contend that an analytical approach is only as good as the assumptions used and that the true utility of an analytical approach is demonstrated when it is shown to match empirical measurements. Weale (2000) has elected an analytical approach that necessarily requires assumptions and data that come from the work of others. Very different conclusions about the utility of this model, than those drawn by Weale (2000), can be made with a closer examination of the data employed.

Weale (2000) mentions equatorial growth of the unaccommodated lens as a factor in presbyopia. Interestingly, this is also considered as a predominant factor in a controversial theory of presbyopia which serves as the basis for which scleral expansion surgery is offered as a cure (Schachar, 1992). To show the age change in lens diameter, Weale (1982) and others (Fincham, 1937; Rafferty, 1985; Schachar, 1992) ironically all cite the same study in which the diameter of isolated human crystalline lenses were measured after excising them from enucleated eyes (Smith, 1883). Weale (1982) also graphs data from a less accessible source (Johansen, 1947: cf Weale, 1982) together with the data from Smith (1883) to show age changes in lens diameter. Since the data from Johansen (1947) is plotted by Weale (1982) together with the data from Smith (1883) and shows the same relationship, it is assumed that lens diameters were measured in the same way in the two studies, i.e. on isolated lenses. This is a reasonable assumption since, until recently, this would have been the only way to measure lens diameter, i.e. in vitro in partly dissected eyes. Weale (1982, 2000), and others (Rafferty, 1985; Schachar, 1992) erroneously consider Smith's (1883) data to represent the diameter of the lens in vivo. Fincham (1937) was cognizant of this difference and of Smith's (1883) recognition of it. Smith (1883) clearly and accurately explained that the diameter of the isolated lens cannot be considered to represent the diameter of the lens in the living eye. von Helmholtz (1909) was also aware of this. Lens diameter has only recently been measured in the living eye with high resolution MRI and shows no age change in the unaccommodated eye (Strenk et al., 1999). The MRI measurements also show a similar increase in accommodated lens diameters with age to Smith's (1883) data (Strenk et al., 1999). Thus, Smith's (1883) data are a good representation of accommodated lens diameter as a function of age. Smith (1883) recognized, as apparently Weale (2000) did not, that when the zonule was cut and the lens isolated, the lens must be considered to be in an accommodated form. When isolated, the lens undergoes a decrease in diameter relatively more so for the young lenses than for the older lenses (Smith, 1883; Fincham, 1937; Glasser & Campbell, 1998; Glasser & Campbell, 1999).

The implications of Weale's (2000) misconception of Smith's (1883) data are: (1) Weale's (2000) analysis leading to the conclusion that there is no zonular shift as described by Farnsworth and Shyne, (1979), but rather a shift of the lens equator 'owing to continued growth' is fundamentally flawed; (2) the use of Smith's (1883) lens diameter data in Weale's (2000) model (Table 1) is inappropriate because Smith's (1883) data describe an accommodative (rather than an age) dependent change in lens diameter; and (3) Weale's (2000) described 'object [of his study] to probe the effect of the

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growth of the lens beyond the ring of zonular insertion on the age related variation in the amplitude of accommodation' cannot be realized with this data because of this misconception on the equatorial growth of the lens.

As an aside, an age dependent increase in thickness of the lens (which is well established from A-scan ultrasonography in the living eye (Weale, 1982; cf. Jansson, 1963) with a constant lens diameter does not preclude an anterior zonular shift with age (Farnsworth & Shyne, 1979; Sakabe, Oshika, Lim, & Apple, 1998). If the posterior lens capsule is thinner than the anterior capsule (Fincham, 1937) and lens growth occurs with an increase in thickness, the posterior capsule will stretch to a greater degree than the anterior capsule. As a consequence, the position of the equatorial zonular/capsular attachment will shift anteriorly on the lens and the distance between zonular insertion and the lens equator will increase in accordance with the results of Farnsworth and Shyne (1979).

Weale (2000), in his model, has used data for Young's modulus of elasticity of the lens obtained from Fisher's (1971) 'refined analytical techniques which are capable of yielding an insight into the underlying processes [of presbyopia] far more readily than is possible from a bulk approach (cf. Glasser & Campbell, 1999)'. However, Fisher's (1971) age dependent increase in Young's modulus of lens elasticity are quite similar to the relative age dependent increase in hardness of the lens (plus capsule) as measured using quite different methods by Glasser and Campbell (1999); Fig. 1. The primary difference between the two is that the data from Fisher (1971) show little increase over the age range 0–50 years during which accommodation declines whereas the data from Glasser and Campbell (1999) show a progressive increase in hardness from birth. The significant exponential relationship fit to this data (Glasser & Campbell, 1999) suggest that from these measurements there is no constancy of lens hardness during the early years. The two sets of data are obtained from very different approaches. Fisher (1971) used a number of inaccurate assumptions to converge

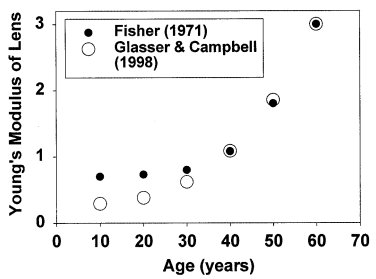

Fig. 1. Young's modulus of the lens matrix from Fisher (1969) as used by Weale (2000), compared with the data of lens resistance to compression forces as measured by mechanically squeezing lenses (Glasser & Campbell, 1999). The latter raw data from Glasser and Campbell (1999) are normalized to the age 60 data of Fisher (1971).

on his values, including assuming a spherical nucleus with a radius equal to the anterior polar depth of the lens (Fisher, 1971). The Young's modulus of elasticity from Fisher (1971) that Weale (2000) uses for the entire lens is for the lens nucleus only. The measurements from Glasser and Campbell (1999) are indeed bulk and include nuclear and cortical contributions, they are obtained from a limited number of lenses and are from axial compressive forces quite unlike the forces on the lens during accommodation. It is certainly unclear if the two sets of measurements are of the same factors or that they are even comparable. Future efforts using more refined techniques may yield better information on how the lens properties change with age (Soergel, Meyer, Eckert, Abele, & Pechhold, 1999).

In order to demonstrate the illegitimacy of the conclusions Weale (2000) draws from his model, it has been recalculated using input data different from those of Weale's (2000); Table 1. For simplicity, this recalculation considers only the case described as dF(90)F&S. This is a computation along the polar axis of the lens, i.e., at $\theta = 90°$ with the zonule inserted at N ($\Theta_c = 20°$; identified as F&S). Since Weale's (2000) alternative conditions show little difference, the other conditions were not tested. However, before this calculation can be attempted, a number of apparent errors in Weale's (2000) Table 1 and Appendix A must be addressed. Weale's (2000) results cannot be replicated with the data and equations as shown. Most fundamentally flawed is Eq. (9).

As given by Weale (2000):

$$\delta = \varepsilon/\sigma \tag{1}$$

where δ is the strain, σ is the stress, and ε is the ratio of capsular and lens elasticity.

The impossible implications of the equation, as given, are that as stress (the force exerted per unit area) increases, strain (the deformation in shape) decreases. This is obviously impossible. In order to replicate Weale's (2000) calculations, it is assumed this equation should have been given as:

$$\delta = \varepsilon \times \sigma \tag{2}$$

and Weale's (2000) Eq. (12) therefore becomes:

$$\mathrm{d}F = \text{constant}\ \varepsilon(1/R) \times \sigma \tag{3}$$

However, Eq. (2) above (and Weale's Eq. (9)) is dimensionally inconsistent. ε is dimensionless. Strain, too is dimensionless, being expressed as the deformation as a proportion of the original dimension. The units of stress are force/area. Weale's (2000) thinking on this relationship requires clarification. In addition, the data in row H of Table 1 and the relationship for k described in Appendix A are also in error.

It is only after these problems are corrected that Weale's (2000) results can be replicated to show the

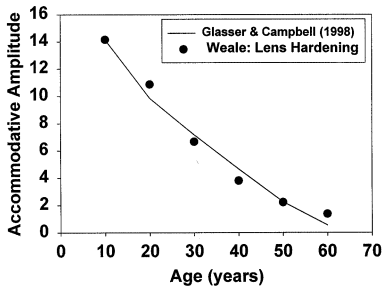

Fig. 2. Data from Weale's (2000) model tested with age independent values for Young's modulus of capsular elasticity, capsular thickness, lens minor and major radii and lens anterior radius of curvature. The values used for Young's modulus of lens elasticity are the scaled values of lens hardness from Glasser and Campbell (1999) (from Fig. 1). These calculated results (solid symbols) are normalized to and plotted with changes in lens power from Glasser and Campbell (1998) (solid line). A RMS value for the two curves as computed by Weale (2000) is 0.275.

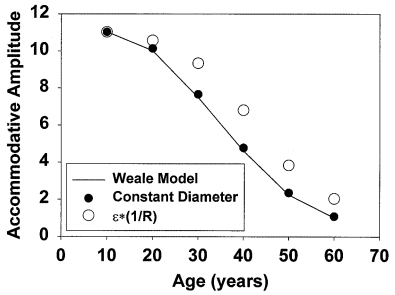

Fig. 3. Graph showing the effect of Weale's (2000) model recalculated with an unchanging lens diameter (Strenk et al., 1999). For simplicity, the model is calculated for only the one condition of dF(90)F&S—i.e. calculated at the lens pole with the zonule position set to 20°—as described by Weale (2000). The solid line is an exact replication of Weale's dF(90)F&S model calculation. The solid symbols are a recalculation of the model with an age independent lens diameter. This demonstrates that an increase in lens diameter, a factor erroneously considered by Weale (2000) to play a role in presbyopia, in fact has negligible influence on the progression of presbyopia as described by his model. A RMS value for the two curves as computed by Weale (2000) is 0.049. A result not substantially different from Weale's original is obtained if the calculated stress (σ) is dropped to give $dF = \varepsilon(1/R)$. In this case the model relies only on Young's modulus and the lens radius of curvature (open symbols).

heavy reliance his model places on just one factor, namely Young's modulus of the lens. These recalculations are not an attempt to prove anything about the etiology of presbyopia since, arguably, there is little to be learned from this model. With the changes noted above, the model was tested with (unjustifiable, but for demonstration purposes) age independent values for Young's modulus of capsular elasticity, capsular thickness, lens minor and major radii and lens anterior radius of curvature. Normalization bring the numbers into physiological range. The only age dependent value used was Young's modulus of elasticity of the lens. The data employed were from Glasser and Campbell's (1999) measurements of lens hardness. The normalized results were plotted with Glasser and Campbell's (1998) results from changes in lens power from mechanical stretching (Fig. 2, solid symbols). In this case the model, all-be-it still using dimensionally inconsistent equations and unjustified age independent values, shows a remarkably good prediction of the loss of 'accommodative ability' of the crystalline lens that Glasser and Campbell (1998) attributed predominantly to hardening of the lens. This exercise is simply to demonstrate the strong dependence that Weale's model places on Young's modulus of elasticity of the lens. Thus, although Weale has argued for a multifactorial contribution to presbyopia, the model he presents relies heavily on lens hardness to predict accommodative loss.

Indeed, so strong a reliance does Weale's model have on Young's modulus of elasticity that if the calculated stress (σ, i.e. Eq. (7)) is eliminated from his Eq. (12) leaving only:

$$dF = \text{constant } \varepsilon(1/R) \tag{4}$$

a recalculation with the original data Weale (2000) employed produces a result not substantially different from his Fig. 4 (Fig. 3). Thus, the very purpose of Weale's (2000) calculated stress (σ) in his Eq. (12) is unclear.

Although Weale believes the increase in lens diameter to contribute some role in presbyopia, a reanalysis of Weale's original model using an age independent lens diameter (Strenk et al., 1999), but with all the other values remaining as per Weale (2000) shows that the model relies not at all on an increase in lens diameter (Fig. 3). The substance of Weale's discussion of the impact of an increase in lens diameter in the progression of presbyopia, an ill founded notion, is seriously undermined.

Weale's (2000) Eq. (3) is apparently an attempt at an equilibrium equation describing the ratio of forces along the lenticular axis to forces acting perpendicular to this. If the capsule is stretched at the lens equator, it will certainly exert a force along the lenticular axis. However the equilibrium of forces achieved along the lenticular axis must also depend on the 'pressure' of the lens substance within the capsule. This pressure seems to have been ignored in Weale's analysis, but clearly cannot be if the analysis is to represent the reality of the lens capsular interactions. Since this interaction is inaccurately described, everything beyond this Eq. (3) should be regarded as incorrect.

Another concern with this type of theoretical analysis is whether the starting point should be based on the accommodated or the unaccommodated lens geometry (Burd, Judge, & Flavell, 1999). When the lens is isolated and the zonular tension removed, the accommodated lens/capsule is at equilibrium. This would represent a stress free state (Burd et al., 1999). An

analysis with this as the starting point would then simply determine the deformation on the lens by applied zonular forces to get the lens into an unaccommodated state. This would be analogous to the mechanical stretching experiments of Glasser and Campbell (1998). So long as the initial accommodated and final unaccommodated geometry of the lens is known, this analysis is possible. However, if the starting point of the analysis is based on the unaccommodated lens geometry, it would first be necessary to know the distribution of stresses on the lens in this unaccommodated state in order to determine how these stresses can act to accommodate the lens to the final equilibrium state. These stresses on the unaccommodated lens cannot be known. This latter approach would be analogous to trying to determine how much a rubber band will shorten when a load is removed. The mechanically more intuitive approach is to ask how much the unloaded rubber band will stretch when the load is applied. It is not entirely clear which starting point Weale's (2000) analysis employs (for it is not stated). However, the data employed by Weale (2000) are an impossible confusion of the two states. Capsular thickness is derived from unloaded capsules (Fisher, 1969), lens diameters from accommodated lenses (Smith, 1883). Lens thickness (Weale, 1982; cf. Jansson, 1963) and radius of curvature (Brown, 1974), however, are from in vivo measurements of unaccommodated eyes. Young's modulus of the capsule is derived from capsule breaking point (Fisher, 1969) and likely very different were it derived from forces closer to the accommodative range (Krag, Olsen, & Andreassen, 1997). Further, Weale's (2000) analysis includes no consideration of the changing geometry of the lens between the accommodated and unaccommodated states, a factor which introduces substantial complexity into this kind of modeling. The use of this inappropriate, mixed data set and the unrealistic simplifications undermine the significance of Weale's calculations and conclusions.

Other inaccuracies in Weale's (2000) work should be identified. Weale (2000) incorrectly and without reference states that the 'the lens, deprived of both zonule and capsule has a smaller radius of curvature than in situ' and that 'if not controlled by the elastic capsule [the lens] tends to revert to its erstwhile more nearly spherical shape. This appears to be true also in its more advancing years'. These unusual and quite possibly unique views of the behavior of the lens and capsule are not in accordance with established facts. Fincham's (1937), Glasser and Campbell's (1998) and Glasser and Campbell's (1999) experimental findings show that the young lens with intact capsule (Fincham: monkey; Glasser & Campbell: human; Glasser unpublished observations: monkey), when freed from zonular tension take on a more accommodated form (von Helmholtz, 1909). This is after all the basis for the accommodative mechanism (von Helmholtz, 1909). In young lenses, when the capsule is then removed, the lens matrix tends to flattens and the surface radii of curvature and focal length increase (Glasser & Campbell, 1999). Older, hardened, presbyopic lenses, unable to undergo accommodative optical changes in vivo (Strenk et al., 1999) and in vitro (Glasser & Campbell, 1998), show essentially no change in shape or focal length when the capsule is removed (Glasser & Campbell, 1999). These empirical results contradict the extraordinary assertions made by Weale (2000). Further, experimental results clearly show that in the young eye, the elastic lens capsule tends to exert a force on the lens substance to hold it in an accommodated form (Glasser & Campbell, 1999). Without the capsule, the lens substance is more like the form of the unaccommodated lens. In situ, the lens is maintained in this unaccommodated form through outward directed zonular tension on the capsule at the lens equator.

Weale (2000) has used the data from Brückner et al. (1987) showing the loss of accommodation as the standard against which his model is tested. His model is for the crystalline lens only; Brückner's accommodation measurements are naturally for the whole eye. Weale's comparison is inappropriate and the closeness of his model data to Brückner's clearly indicate a departure from reality. Although Glasser and Campbell (1998) compared accommodation of the lens with accommodation of the eye, they recognized and discussed the difference. A change in power of the crystalline lens produces a 20% less change in power of the eye (Bennett & Rabbetts, 1989; Glasser & Campbell, 1998). Therefore, were the Weale (2000) model to be truly predictive, it should fall below the Brückner et al. (1987) in vivo accommodative amplitudes, relatively more so for the younger lenses. Since Weale (2000) models accommodative change in lens power, the recalculations are more appropriately compared to the lens power changes measured by Glasser and Campbell (1998) (Fig. 2).

Thus, in addition to a number of other errors in the manuscript, Weale (2000), in his analytical approach, has used data for lens diameters that are demonstrably incorrect, has rejected Glasser and Campbell's (1999) measurements of lens hardness as inaccurate yet used data that are remarkably similar, has drawn inappropriate comparisons, has used dimensionally inaccurate equations and has expressed unsubstantiated and inaccurate statements. This reanalysis of Weale's model provides a demonstration that an analytical approach is only as good as the data used to test it and that the true utility of such an approach is only realized when the model can be shown to accurately predict the empirical measurements.

Since the validity of this model is not unequivocal, this study does not, as Weale claims, clearly resolve the

apparent conundrum of the relatively rapid decline in accommodation. On the basis of the model presented, it is not at all clear that presbyopia can be fully explained by a multifactorial component contribution of normal aging of the component elements of the accommodative apparatus. This is by no means meant to suggest that presbyopia can be attributed purely to change in lens hardness or any other single factor for that matter. A wealth of studies show age change in the extralenticular apparatus (see Glasser & Campbell, 1998) and these must certainly impact on the inability of the aged eye to accommodate. New studies and lively debate continues to contribute to what we know and understand about presbyopia. It is important is that the studies continue, that they remain judicious and the debate remain lively, but well founded on sound scientific principles.

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